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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,081	09/25/2006	Paul Gregor	GREGOR8	8816

1444 7590 10/25/2007

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER
THOMAS, TIMOTHY P

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,081	GREGOR ET AL.	
	Examiner	Art Unit	
	Timothy P. Thomas	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,18-22,29-32,43-46,63-66 and 73-85* is/are pending in the application.

4a) Of the above claim(s) *18,19,21,43,45,46,63-66,73,74,76,78 and 80-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,20,22,29-32,44,75,77,79 and 85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on 9/21/2007 is acknowledged. The traversal is on the ground(s) that the disclosed compound by Selwood, et al. (WO 01/32604 A1; previously cited) no longer reads on the claims, since applicant has filed a preliminary amendment to the claims (9/20/2007), which specifically excludes the compound cited from Selwood. This is not found persuasive because the amended claim set, filed 9/25/2006, on which the restriction requirement is based, lacks unity of invention for the reason of record. Additionally, while it is noted that some of the claims have been amended to exclude the Selwood compound, claim 1 has not, and still reads on this compound, as outlined in the restriction requirement. Although not required for the lack of unity determination, it is pointed out that Selwood does teach pharmaceutical compositions with diluents and carriers (see p. 37); and thus anticipates claim 1. Since a specie anticipating the claims has been disclosed in the prior art, the lack of unity of the instant claim set remains and the restriction requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicant's election with traverse of compound No. 2011 as the single disclosed compound specie and acute and chronic inflammation (with the more specific condition of rheumatoid arthritis) as the species of disease, disorder or condition in the reply filed on 9/21/2007 is acknowledged (Note: "acute and chronic inflammation" will be considered an elected subgenus with rheumatoid arthritis as the elected disease

specie). Claims identified as encompassing the elected compound specie are 20, 22, 29-32, 44, 46, 65, 73, 74, 75, 77-80, and 82-85; claims that encompass the elected disease specie are 22, 29-32, 46, 63-66, 73, 74, 77, 79-83, 85 and those that do not mention and treatment (generic to all treatments). The traversal is on the ground(s) that the disclosed compound cited from Selwood no longer applies, since the claims have been amended to exclude the cited compound. This is not found persuasive because the amended claim set, filed 9/25/2006, on which the restriction requirement is based, lacks unity of invention for the reason of record, and claim 1 still reads on the disclosed compound and composition.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 46, 63-66, 73-74, are 80-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/21/2007.

4. Claims 18-19, 21, 43, 45, 76 and 78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/21/2007.

Status of Claims

5. Claims 1, 20, 22, 29-32, 44, 75, 77, 79 and 85 are examined on the basis of the merits.

Priority

6. Applicant has requested acknowledgment of Applicant's papers filed under paragraph 119. It appears that applicant is referring to the claim for priority under 35 U.S.C. 119(e) to Application No. 60/555667, claimed in the Application Data Sheet filed 9/25/2006.

7. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/555667, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

The elected compound specie, Compound No. 2011 (as well as Compounds No. 2010 and 2012; claims 19-21, 43-45), does not appear in the priority document 60/555667, and therefore claims 19-21 and 43-45 are accorded the later priority date of the PCT application, PCT/IL05/00336, filed 3/24/2005.

Specification

8. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

9. The abstract of the disclosure is objected to because of the use of legal phraseology, “comprising”, in the 1st line. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Regarding claim 77, the phrase "such as", used multiple times and “particularly”, 9 lines from the end of the claim, renders the claim indefinite because it is unclear

whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 22 and 77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for about a 50% inhibition of L-Selectin binding to Heparin using the active compounds in the compositions of the instant claims, does not reasonably provide enablement for treatment or "prevention" of inflammatory or autoimmune diseases, disorders, or diseases, such as rheumatoid arthritis, lupus, multiple sclerosis, hepatitis C and AIDS. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has claimed applicability of the compositions to treat and prevent a broad range of diseases with different characteristics and causes; for instance, rheumatoid arthritis, a disease of the joints with associated pain and deformity vs. hepatitis C, a viral infection. Use of the compositions in efficacious treatment of any of these diseases would require undue experimentation to identify effective compounds for each of these diseases. No evidence has been provided that prevention of any disease claimed is a potential property of any of the claimed compounds.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation,

such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a pharmaceutical composition for the treatment or prevention of various inflammatory or autoimmune diseases, disorders or conditions, selected from a broad genus of diseases in the dependent claim 77. Thus, the claims taken together with the specification imply that the use of any compound of formula 1 will be effective for treating and preventing every one of the named diseases, such as rheumatoid arthritis, lupus, multiple sclerosis, hepatitis C and AIDS.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Sharma, et al. ("Biologics in rheumatoid arthritis."; 2004; J. Assoc. Physicians India; 52: 231-6; abstract) teaches a satisfactory remission of rheumatoid arthritis is seldom achieved; that may patients fail to gain a satisfactory response to drugs that are the treatment of choice and some therapy may raise the risk of serious infections. The art is unpredictable as to which drugs will be effective in such treatments, and even more unpredictable in identifying drugs that will prevent these conditions.

(5) The relative skill of those in the art:

The relative skill in the art is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for using the instant compositions to partially inhibit L-selectin binding to heparin.

However, the specification does not provide guidance or evidence to support effective treatment or prevention of any of the claimed diseases, nor factors that may be used to select an appropriate compound.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to treatment, remission and satisfactory response to current drugs in rheumatoid arthritis and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1, 20, 22, 29-32, 44, 75, 77, 79, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ivachtchenko, et al. ("Synthesis of Substituted 4-Oxo-2-thioso-1,2,3,4-tetraquinazolines and 4-Oxo-3,4-dihydroquinazoline-2-thioles"; 2003 Aug; J. Comb. Chem. 5: 775-788).

Ivachtchenko teaches the synthesis of combinatorial libraries of various substituted core structures, including the core structure of Formula 1 of claim 1, 4-oxo-3,4-dihydroquinazoline-2-thiole (structure 2{3(1-734)}; Figure 1); substitutions in position R3 or R4 of Formula I include the (1H-imidizol-1-yl)propyl moiety and H in the other

position (R3/R4 of Compound 2011; 7{33}, Figure 5; 7{81}, Figure 11); compound 11{8} (Figure 10) shows nearly the same moiety (phenylethyl) as R1 in instant Figure 1 for the elected Compound No. 2011 (the elected R1 moiety is phenylmethyl) attached to the same core structure (a keto-enol variant of the –SH form); the phenylmethyl moiety is shown in the reactant form (alkylchloride) in 13{21} (Figure 14); structure 2{1(2)} shows a structure of Figure 1 with the [(5-acetyl-2-methoxyphenyl)methyl]thiol moiety for R2 (same as the elected Compound 2011; Figure 19); a systematic variation in substituents is taught to synthesize a library of compounds for biological testing (abstract; p. 775, 1st paragraph). Ivachtchenko does not teach the elected Compound No. 2011. It would have been obvious to one of ordinary skill in the art at the time of the invention to attach the above identified substituents taught by Ivachtchenko to the core structure taught by Ivachtchenko to synthesize the elected Compound No. 2011, of claim 44, as well as many other compounds of Formula I, with an expectation of success. The motivation to do so is taught by Ivachtchenko, that these compounds possess a wide range of biological activities and provide an incentive for further exploration of this class of compounds as potential drug precursors (p. 775, 1st paragraph). It would also have been obvious to prepare a pharmaceutical composition suitable for in vitro and in vivo biological testing containing the active compound and a pharmaceutically acceptable diluent and/or carrier, also with the motivation of exploring the biological activities for potential drug use.

A pharmaceutical composition, so prepared for biological effectiveness, would be suitable for and have the activities recited in claims 22, 29-32, 77 and 79 as inherent

propertie, as disclosed by applicant. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Conclusion

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TPT/
Timothy P. Thomas
Patent Examiner

Ardin H. Marschel 10/21/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER